



Development Support Document  
Final, April 15, 2008

# **Tetrachloroethylene (PCE)**

**CAS Registry Number: 127-18-4**

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TEXAS COMMISSION ON ENVIRONMENTAL QUALITY

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## Chapter 1 Summary Tables

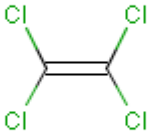
Table 1 provides a summary of health- and welfare-based values from an acute and chronic evaluation of tetrachloroethylene (PCE) can be found in Table 1. Table 2 provides summary information on PCE's physical/chemical data.

<b>Table 1. Health- and Welfare-Based Values</b>		
<b>Short-Term Values</b>	<b>Concentration</b>	<b>Notes</b>
<sup>acute</sup> ESL [1 h] (HQ = 0.3)	2,000 $\mu\text{g}/\text{m}^3$ (300 ppb) <b>Short-Term ESL for Air Permit Reviews</b>	<b>Critical Effect(s):</b> latency of pattern reversal visual-evoked potential and performance deficits for eye-hand coordination in human volunteers
acute ReV (HQ = 1)	6,800 $\mu\text{g}/\text{m}^3$ (1,000 ppb) <sup>a</sup>	
<sup>acute</sup> ESL <sub>odor</sub>	5,200 $\mu\text{g}/\text{m}^3$ (770 ppb) <sup>a</sup>	50% odor detection, ethereal chlorinated solvent odor
<sup>acute</sup> ESL <sub>veg</sub>	---	No data found
<b>Long-Term Values</b>	<b>Concentration</b>	<b>Notes</b>
<sup>chronic</sup> ESL <sub>nonlinear(nc)</sub> (HQ = 0.3)	110 $\mu\text{g}/\text{m}^3$ (16 ppb)	<b>Critical Effect(s):</b> decreased in automated and manual hematocrit values, hemoglobin, and erythrocyte counts in rats and mice
chronic ReV (HQ = 1)	370 $\mu\text{g}/\text{m}^3$ (54 ppb) <sup>a</sup>	
<sup>chronic</sup> ESL <sub>linear(c)</sub>	26 $\mu\text{g}/\text{m}^3$ (3.8 ppb) <sup>a, b</sup> <b>Long-Term ESL for Air Permit Reviews</b>	<b>Critical Effect(s):</b> increase in the incidences of hepatocellular carcinomas in mice and rats
<sup>chronic</sup> ESL <sub>veg</sub>	82 $\mu\text{g}/\text{m}^3$ (12 ppb) <sup>a</sup>	<b>Critical Effect(s):</b> decrease in dry weight of pod, ear and shoot, and pod yield; increase in stem diameter; or foliar injury in various plant species

<sup>a</sup> Values that may be used for evaluation of air monitoring data

<sup>b</sup> Unit risk factor (URF) =  $3.8 \times 10^{-7}$  per  $\mu\text{g}/\text{m}^3$  ( $2.6 \times 10^{-6}$  per ppb)

Abbreviations: **HQ**, hazard quotient; **ppb**, parts per billion;  $\mu\text{g}/\text{m}^3$ , micrograms per cubic meter; **h**, hour; **ESL**, Effects Screening Levels; **ReV**, Reference Value; <sup>acute</sup>ESL, acute health-based ESL; <sup>acute</sup>ESL<sub>odor</sub>, acute odor-based ESL; <sup>acute</sup>ESL<sub>veg</sub>, acute vegetation-based ESL; <sup>chronic</sup>ESL<sub>linear(c)</sub>, chronic health-based ESL for linear dose-response cancer effect; <sup>chronic</sup>ESL<sub>nonlinear(nc)</sub>, chronic health-based ESL for nonlinear dose-response cancer effect; <sup>chronic</sup>ESL<sub>nonlinear(nc)</sub>, chronic health-based ESL for nonlinear dose-response noncancer effects; <sup>chronic</sup>ESL<sub>linear(nc)</sub>, chronic health-based ESL for linear dose-response noncancer effects; and <sup>chronic</sup>ESL<sub>veg</sub>, chronic vegetation-based ESL

<b>Table 2. Chemical and Physical Data</b>		
<b>Parameter</b>	<b>Value</b>	<b>Reference</b>
Molecular Formula	C <sub>2</sub> Cl <sub>4</sub>	ACGIH 2001
Chemical Structure		ChemIDplus
Molecular Weight	165.8	ACGIH 2001
Physical State	Liquid	ACGIH 2001
Color	Colorless, clear	ACGIH 2001
Odor	ethereal odor	ACGIH 2001
CAS Registry Number	127-18-4	ACGIH 2001
Synonyms	Perchloroethylene, 1,1,2,2-tetrachloroethylene, perchlor, perclene, tetrachloroethene, PERC, PCE	ACGIH 2001
Solubility in water	practically insoluble (206 mg/L)	ChemIDplus
Log P <sub>ow</sub>	3.4 (octanol-water)	ChemIDplus
Vapor Pressure	18.5 mmHg @20°C	ChemIDplus
Relative Vapor Density (air = 1)	5.8 g/cc	Verschueren 2001
Relative Density (water = 1)	1.625 at 20°C	ACGIH 2001
Melting Point	-22.4°C	ACGIH 2001
Boiling Point	121°C	ACGIH 2001
Conversion Factors	1 μg/m <sup>3</sup> = 0.15 ppb @ 25°C 1 ppb = 6.8 μg/m <sup>3</sup>	ACGIH 2001

## **Chapter 2 Major Uses or Sources**

PCE is generally used in a variety of applications. It is widely used as a solvent in the dry-cleaning and vapor-degreasing industry; as solvents for fats, greases, waxes, rubber, gums, and removing caffeine from coffee; as a drying agent for metals and certain other solids; as a medium for transferring heat; and in the manufacture of paint removers and printing inks, trichloroacetic acid, and fluorocarbons (ACGIH 2001 and Verschueren 2001).

## **Chapter 3 Acute Evaluation**

### ***3.1 Health-Based Acute ReV and ESL***

#### **3.1.1 Physical/Chemical Properties**

PCE is a colorless liquid with an ethereal odor (refer to Section 3.3.1). It is practically insoluble in water. The main chemical and physical properties of PCE are summarized in Table 2.

#### **3.1.2 Key Studies**

Acute inhalation exposure to PCE in humans has resulted in intense irritation of the upper respiratory tract and eyes, kidney dysfunction, neurological effects such as reversible mood and behavioral changes, impairment of coordination, aesthetic effects, and liver toxicity (ATSDR 1997, USEPA 2003).

In one study, four human volunteers were sequentially exposed to 106, 216, 280, 600, or 1060 ppm PCE vapor for various time periods (Rowe et al. 1952). Exposure to 106 ppm for approximately 1 hour (h) resulted in slight eye irritation, detection of an odor, and dizziness and drowsiness; exposure to as low as 216 ppm for 45 minutes to 2 hours (h) resulted in more severe eye and nasal irritation and central nervous system effects. In another study by Stewart et al. (1961b in ATSDR 1997), transient eye irritation was noted in 6 human subjects during the first few minutes of exposure at 75-80 ppm.

Human subjects exposed to 100 ppm PCE for 7 h displayed symptoms such as headache and dizziness and exhibited CNS effects as indicated by an abnormal Romberg test of position balance (Stewart et al. 1970). Symptoms were noted after the first 3 h of exposure. There were drawbacks in this study. First, only one exposure concentration (100 ppm) was used. In addition, no control subjects were included.

The most sensitive target organ in humans exposed to PCE by inhalation is the central nervous system (CNS). Numerous acute neurological effects of inhaled PCE in human and animal studies have been reported. The acute ESL was based on a well designed human inhalation study by Altmann et al. (1992), despite the fact that an unexposed control group was not included. Neurological function tests were studied in 28 male volunteers exposed to PCE at 10 or 50 ppm for 4 h/day for 4 days. Significantly increased latency of pattern reversal visual-evoked potential (VEP) and significant performance deficits for vigilance and eye-hand coordination were observed in 16 volunteers exposed at 50 ppm, compared to 12 volunteers exposed at 10 ppm. The study authors concluded that the increased peak latencies of the VEPs suggest interference with nerve cell conduction and could be due to a variation in the arousal level

or to a direct solvent-induced cortical depression. A no-observed-adverse-effect level (NOAEL) of 10 ppm was identified from this study and was used as the point of departure (POD).

### **3.1.3 Additional Supportive Acute Neurological Toxicity Data**

Dizziness/sleepiness was reported in volunteers exposed to concentrations as low as 216 ppm for 45 minutes to 2 h; and loss of motor coordination occurred with exposure at 280 ppm for 2 h or at 600 ppm for 10 minutes (Rowe et al. 1952). A NOAEL of 106 ppm for neurological effects was identified from this study.

Abnormal position sense was observed in 17 human volunteers exposed to 100 ppm PCE vapor for 7 h, and symptoms of headache and light-headedness were noted in three subjects after the first 3 h of exposure (Stewart et al. 1970).

In another study conducted by Stewart et al. (1981), cerebral control depression was observed during the first day of exposure at 100 ppm in 4 male volunteers sequentially exposed to 0, 20, 100, or 150 ppm PCE vapor for 7.5 h/day, 5 days/week. A NOAEL of 20 ppm for CNS effects was identified from this study. While the NOAEL of 20 ppm is the highest reported NOAEL identified from human studies thus far, the Stewart et al. (1981) study was limited by the small number of subjects that were investigated and no control subjects were included. The TS believes the NOAEL of 10 ppm identified from the Altmann et al. (1992) study is more appropriate and conservative to be used as POD (see Section 3.2.1).

### **3.1.4 Mode-of-Action Analysis and Dose Metric**

The mode of action (MOA) for CNS effects has not been clearly established but may be related to solvent effects on lipid and fatty acid compositions of membranes. Since the key study is based on human volunteer exposure, exposure concentration of the parent chemical will be used as the dose metric.

### **3.1.5 Critical Effect and Dosimetric Adjustments**

A NOAEL (for neurological function) of 10 ppm identified from the Altmann et al. (1992) study was used as the  $POD_{HEC}$  because it had the lowest observed NOAEL. Since there is not sufficient evidence to show that the neurological effects of PCE are both concentration and duration dependent, and the exposure duration of the key study (4 h) is less than 8 h, no exposure duration adjustment is conducted (TCEQ 2006). Therefore, the unadjusted  $POD_{HEC}$  was conservative.

### **3.1.6 Adjustments of $POD_{HEC}$ to Health-Based Acute ReV and <sup>acute</sup>ESL**

The acute Reference Value (ReV) of 1,000 ppb ( $6,800 \mu\text{g}/\text{m}^3$ ) was derived by applying an uncertainty factor (UF) of 10 for human variability to the  $POD_{HEC}$  of 10 ppm. A UF of 1 was used for database uncertainty because the overall quality of the studies is high. The <sup>acute</sup>ESL of 300 ppb ( $2,000 \mu\text{g}/\text{m}^3$ ) was set according to the ESL guidance (TCEQ 2006) based on the acute ReV of 1,000 ppb multiplied by a hazard quotient (HQ) of 0.3 (Table 3).

<b>Table 3. Derivation of the Acute ReV and <sup>acute</sup>ESL</b>	
Study	Altmann et al. 1992
Study population	28 healthy male volunteers
Key Study Confidence Level	Medium
Exposure Method	exposure via inhalation at 10 or 50 ppm
Critical Effects	CNS Effects- latency of pattern reversal visual-evoked potential and performance deficits for eye-hand coordination
POD	10 ppm (NOAEL)
Exposure Duration	4 h/day for 4 days
Extrapolation to 1 h	No adjustment, 1 h concentration = 4 h concentration (Section 3.2.4)
Extrapolated 1 h concentration	10 ppm
Total uncertainty factors (UFs)	10
<i>Interspecies UF</i>	N/A
<i>Intraspecies UF</i>	10
<i>LOAEL UF</i>	N/A
<i>Incomplete Database UF</i>	1
<i>Database Quality</i>	High
<b>Acute ReV (HQ = 1)</b>	<b>6,800 <math>\mu\text{g}/\text{m}^3</math> (1,000 ppb)</b>
<b><sup>acute</sup>ESL (HQ = 0.3)</b>	<b>2,000 <math>\mu\text{g}/\text{m}^3</math> (300 ppb)</b>

### ***3.2 Welfare-Based Acute ESLs***

#### **3.2.1 Odor Perception**

PCE has an ethereal chlorinated solvent odor. Leonardos et al. (1969) reports the 100% recognition odor threshold as 4.68 ppm (31.74  $\text{mg}/\text{m}^3$ ). May (1966) reports the odor detection and recognition threshold values as 47 and 71 ppm, respectively. These published values have been reviewed and accepted by the American Industrial Hygiene Association (AIHA) and United States Environmental Protection Agency (USEPA) according to their acceptance criteria. In addition, Nagata (2003) reports a 50% detection odor threshold value of 770 ppb, which is lower than the Leonardos et al. (1969) or May (1966) studies. The measurement of PCE odor threshold by Nagata (2003) meets the TCEQ guidelines to develop odor-based ESLs (TCEQ 2006). Thus, the odor-based ESL is set at the lowest accepted odor threshold concentration of 770 ppb (5,200  $\mu\text{g}/\text{m}^3$ ). The proposed  $\text{ESL}_{\text{odor}}$  of 770 ppb is deemed appropriate and is comparable to the odor threshold of 1,000 ppb reported by ATSDR (1997).

### 3.2.2 Vegetation Effects

Possible acute effects of PCE on plants have been investigated by Frank and Frank (1986) (in European Union 2005). Single needles from spruce trees were exposed to PCE under direct irradiation for 5 h and found that the needles changed color from dark green to a dirty brown green. However, there were several drawbacks in this study such as the uses of direct UV radiation, uncontrolled exposures, and possible presence of other pollutants (sulfur dioxide and nitrogen dioxide); the authors concluded that it was not possible to derive statistical values from their study. The acute data was considered insufficient to indicate that special consideration should be given to possible vegetation effects from short-term exposure to PCE.

### 3.3 Short-term ESL and Values for Air Monitoring Evaluation

This acute evaluation resulted in the derivation of the following acute values:

- acute ReV =  $6,800 \mu\text{g}/\text{m}^3$  (1,000 ppb)
- $^{\text{acute}}\text{ESL} = 2,000 \mu\text{g}/\text{m}^3$  (300 ppb)
- $^{\text{acute}}\text{ESL}_{\text{odor}} = 5,200 \mu\text{g}/\text{m}^3$  (770 ppb)

The short-term ESL for air permit evaluations is the health-based  $^{\text{acute}}\text{ESL}$  of  $2,000 \mu\text{g}/\text{m}^3$  (300 ppb) (Table 1). For evaluation of air monitoring data, the  $^{\text{acute}}\text{ESL}_{\text{odor}}$  of  $5,200 \mu\text{g}/\text{m}^3$  (770 ppb) is lower than the acute ReV of  $6,800 \mu\text{g}/\text{m}^3$  (1,000 ppb), although both values may be used for the evaluation of ambient air monitoring data (Table 1). The  $^{\text{acute}}\text{ESL}$  (HQ = 0.3) is not used to evaluate ambient air monitoring data.

## Chapter 4 Chronic Evaluation

### 4.1 Noncarcinogenic Potential

Animal studies have reported noncarcinogenic effects on the liver, kidney, and CNS from subchronic and chronic inhalation exposure to PCE. The major chronic noncarcinogenic effects in humans are neurological effects, including headaches, and impairment of color vision, visual spatial function, memory, concentration, and intellectual function (ATSDR 1997, USEPA 2003). While some adverse reproductive effects, such as menstrual disorders and spontaneous abortions, have been reported from occupational exposure to PCE, no definite conclusions can be made because of the limitations of the studies (ATSDR 1997).

#### 4.1.1 Key Study

The major noncarcinogenic effects from chronic inhalation exposure to PCE in humans are neurological effects, including headaches, and impairment of memory, concentration, and intellectual function. The  $^{\text{chronic}}\text{ESL}_{\text{nonlinear(nc)}}$  was based on a human inhalation study by Ferroni et al. (1992). Neurobehavioral effects were studied in 60 women who worked in dry cleaning shops at an average concentration of 15 ppm PCE for an average of 10.1 years. Significant increases in simple reaction times ( $p < 0.0001$ ), impaired vigilance ( $p < 0.005$ ), and stress ( $p < 0.005$ ) were observed in the dry cleaners when compared with the 30 unexposed, matched controls. Additionally, the mean serum level of prolactin was significantly higher in the workers than in the matched controls ( $p < 0.001$ ). The study authors concluded that PCE exposure in dry cleaning shops may impair performance and affect pituitary function but that the cross-sectional design prevents distinguishing acute effects from chronic effects. Such selection bias would lead to an underestimate of the actual or underlying risk (USEPA 2003). Nevertheless, the study was considered well-conducted, e.g., sizes of study subjects for both workers and controls are large;

workplace air samples were well conducted; both groups were similar in height, weight, smoking habits, use of medication, and low level of daily alcohol intake; PCE blood levels as well as serum prolactin levels were measure, and five neurobehavioral tests were examined in all subjects. A lowest-observed-adverse-effect level (LOAEL) of 15 ppm was identified from this study and was used as the occupational exposure POD (POD<sub>OC</sub>). No NOAEL was identified from this study.

#### 4.1.2 Additional Supportive Studies

In a study of 26 dry cleaning workers in Belgium exposed to a time-weighted average (TWA) concentration of 21 ppm PCE (range from 9 to 38 ppm) over an average of 6.4 years, no significant alterations were detected in neurological symptoms or psychomotor performances compared to 33 unexposed controls (Lauwerys et al. 1983 in ATSDR 1997 and USEPA 2003). However, 13 of the 26 dry cleaning workers participated in this study, compared to only 9 of the 33 controls, were smokers (USEPA 2003).

In another study, Cai et al. (1991 in ATSDR 1997 and USEPA 2003) reported an increase in subjective symptoms including dizziness and forgetfulness in workers exposed to PCE at geometric mean concentration of 20 ppm (range from 4 to 97 ppm) for a mean duration of 36 months (range from 1 to 120 months) relative to controls.

In another study (Altmann et al. 1995), the effects of chronic low-level PCE exposure on functions of the CNS were measured in 19 persons chosen from a population of 92 subjects living in the neighborhood of dry cleaning shops with a mean residence time of 10.6 years. A total of 30 controls were selected from volunteers who had no history of solvent exposure. Neurobehavioral tests were performed using a neurological battery and pattern reversal VEPs were recorded. The median value of the indoor air concentration was 1.36 mg/m<sup>3</sup> (0.21 ppm) [mean ± SD: 4.98 ± 6.78 mg/m<sup>3</sup> (0.74 ± 1.02 ppm)] for the exposed group and 1.8 µg/m<sup>3</sup> (mean ± SD: 3.36 ± 3.29 µg/m<sup>3</sup>) for the control group. The mean blood PCE concentration measured in the examination room was 17.8 µg/L in exposed subjects and below the detection limit of 0.5 µg/L in controls. Statistically significant differences were observed between the responses of the exposed and control subjects in the battery tests for vigilance, simple reaction time, as well as visual memory, whereas no statistically significant differences were observed for VEP latencies. The study authors concluded that long-term PCE exposure in subjects living near a dry cleaning shop may affect CNS functions. The authors, however, acknowledged that the study was limited by the small number of subjects that were investigated.

#### 4.1.3 Mode-of-Action Analysis and Dose Metric

The MOA for CNS effects has not been clearly established but may be related to solvent effects on lipid and fatty acid compositions of membranes. Since the key study is based on occupational exposure, exposure concentration of the parent chemical will be used as the dose metric.

#### 4.1.4 Critical Effect and Dosimetric Adjustments

A LOAEL (neurobehavioral effects) of 15 ppm identified from the Ferroni et al. (1992) study was used as POD<sub>OC</sub> because the quality of the study was superior to other key studies. To convert from occupational exposure to continuous exposure relevant to the general population (POD<sub>HEC</sub>), the POD<sub>OC</sub> of 15 ppm was multiplied by a dosimetric adjustment factor for exposure continuity using default occupational and nonoccupational ventilation rates and exposure frequencies (TCEQ 2006):

$$\text{POD}_{\text{HEC}} = \text{POD}_{\text{OC}} \times (\text{VE}_{\text{ho}}/\text{VE}_{\text{h}}) \times (\text{days per week}_{\text{oc}}/\text{days per week}_{\text{res}})$$

where:  $\text{VE}_{\text{ho}}$  = occupational ventilation rate for an 8-h day (10 m<sup>3</sup>/day)

$\text{VE}_{\text{h}}$  = non-occupational ventilation rate for a 24-h day (20 m<sup>3</sup>/day)

days per week<sub>oc</sub> = occupational weekly exposure frequency (study specific)

days per week<sub>res</sub> = residential weekly exposure frequency (7 days per week)

$$\text{POD}_{\text{HEC}} = 15 \text{ ppm} \times [10/20 \text{ m}^3 \text{ day}] \times [5 \text{ d}/7 \text{ d}] = 5.36 \text{ ppm}$$

#### **4.1.5 Adjustments of $\text{POD}_{\text{HEC}}$ to Chronic ReV and $\text{chronic ESL}_{\text{nonlinear(nc)}}$**

The chronic ReV of 54 ppb was calculated by applying both a LOAEL-to-NOAEL UF of 10 and an intraspecies UF of 10 to account for human variability to the  $\text{POD}_{\text{HEC}}$  of 5.36 ppm. The average exposure duration of 10.1 years in the Ferroni et al. (1992) study is more than 10% of the life span in humans; therefore the study would be considered to be a chronic study, thus a UF of 1 was used to account for the exposure duration. A UF of 1 was also used for database uncertainty because the overall quality of the studies is high. The  $\text{chronic ESL}_{\text{nonlinear(nc)}}$  of 16 ppb was set according to the ESL guidance (TCEQ 2006) based on the chronic ReV of 54 ppb multiplied by a HQ of 0.3 (Table 4).

<b>Table 4. Derivation of the Chronic ReV and <sup>chronic</sup>ESL<sub>nonlinear(nc)</sub></b>	
Study	Ferroni et al. 1992
Study population	60 female workers in dry cleaning shops
Key Study Confidence Level	Medium to high
Exposure Method	Workplace inhalation
Critical Effects	Behavioral effects: increased reaction times
POD <sub>OC</sub>	15 ppm (LOAEL)
Exposure Duration	8 h/day, 5 days/week, for an average of 10.1 years
POD <sub>HEC</sub> Dosimetry adjustment from occupational to general population	$15 \text{ ppm} \times [10/20 \text{ m}^3 \text{ day}] \times [5\text{d}/7\text{d}] = 5.36 \text{ ppm} (5,360 \text{ ppb})$
Total UFs	100
<i>Interspecies UF</i>	N/A
<i>Intraspecies UF</i>	10
<i>LOAEL UF</i>	10
<i>Subchronic to chronic UF</i>	1
<i>Incomplete Database UF</i>	1
<i>Database Quality</i>	High
<b>Chronic ReV (HQ = 1)</b>	<b>370 <math>\mu\text{g}/\text{m}^3</math> (54 ppb)</b>
<b><sup>Chronic</sup>ESL<sub>nonlinear(nc)</sub> (HQ = 0.3)</b>	<b>110 <math>\mu\text{g}/\text{m}^3</math> (16 ppb)</b>

## 4.2 Carcinogenic Potential

### 4.2.1 Carcinogenic Weight of Evidence

Epidemiological studies have shown mixed results for the carcinogenicity of PCE; some studies reported an increased incidence of a variety of tumors, while other studies did not report any carcinogenic effects (CDHS 1991). In a recent comprehensive review of the epidemiological literature on occupational exposure to PCE and cancer, Mundt et al. (2003) concluded that the current epidemiological evidence does not support a conclusion that occupational exposure to PCE is a risk factor for cancer of any specific site. Specifically, the authors found no evidence for or unlikely association between several important cancer types and exposure to PCE. Scientific evidence was inadequate for laryngeal, kidney, esophageal and bladder cancers.

In a more recent epidemiological study by Lynge et al. (2006), a series of case-control studies nested in cohorts of 46,768 laundry and dry cleaning workers from the 1970 census in four Nordic countries was investigated. The results showed that the risks of cancer of the esophageal, gastric cardiac, liver, pancreas, and kidney and non-Hodgkin lymphoma were not significantly increased among the Nordic dry cleaners. The authors found an excess risk of bladder cancer that was not associated with PCE exposure.

In animal studies, two chronic bioassays, an oral gavage study (NC1 1977 in ATSDR 1997) and an inhalation study (NTP 1986), have been conducted in rodents to assess the potential carcinogenicity of PCE. The tumor data observed in these two studies have been used in the carcinogenic risk assessment for PCE. The USEPA classified PCE as a Group B2/C: Probable human carcinogen of low carcinogenic hazard based on the 1986 cancer guidelines (USEPA 1986a). This was based on sufficient evidence from animal studies and inadequate evidence or no data from epidemiologic studies. Using the weight-of-evidence narrative recommended in the 2005 cancer guidelines (USEPA 2005a), the TCEQ has classified PCE as “Likely to Be Carcinogenic to Humans via Inhalation” (TCEQ 2006).

#### 4.2.2 Key Studies

The National Toxicology Program (NTP) reported the results of an inhalation study in which F344/N rats and B6C3F1 mice were exposed to PCE at 0, 200 or 400 ppm (rats) or 0, 100 or 200 ppm (mice) 6 h/day, 5 days/week for 103 weeks (NTP 1986). In this study, male F344/N rats showed a statistically significant increase in the incidence of mononuclear cell leukemia and a dose-related trend for rare renal tubular neoplasm. Female rats showed a statistically significant increase in the incidence of mononuclear cell leukemia. In mice, PCE induced a statistically significant increase in the incidence of hepatocellular adenomas or carcinomas at both treatment concentrations. In rats, PCE produced no increase in the incidence of hepatocellular carcinomas in the females and a slight but not statistically significant increase in the males.

While the current epidemiological evidence does not support a conclusion that occupational exposure to PCE is a risk factor for cancer of any specific site including liver cancer, there are limitations among available studies, e.g., confounding factors, widespread lack of valid exposure data, etc (Mundt et al. 2003, Lynge et al. 2006). Additionally, tumor data observed from the NTP (1986) animal studies strongly show that PCE is carcinogenic in animals. Therefore, the TS conservatively used the results from the 1986 NTP inhalation bioassay to develop the  $^{chronic}ESL_{linear(c)}$ .

#### 4.2.3 Mode-of-Action Analysis

The MOA for liver toxicity including cancer in mice is thought to be the induction of peroxisome proliferation (and resulting increases in hydrogen peroxide and oxidative damage) by trichloroacetic acid (TCA), a metabolite of PCE. An alternative MOA suggests that liver toxicity is due to cytotoxicity associated with reactive intermediates produced during the oxidative metabolism of PCE (Clewell et al. 2005). However, because humans produce little TCA following PCE exposure and because the peroxisome proliferation response in humans is minimal, liver hypertrophy and tumor development as it is observed in mice may not occur by the same mechanism in humans (ATSDR 1997). Because MOA does not indicate whether the dose-response shape is linear (non-threshold) or non-linear (threshold), we defaulted to linear (non-threshold) and developed a  $^{chronic}ESL_{linear(c)}$  (TCEQ 2006).

## 4.2.4 Dosimetric Adjustments and Dose-Response Assessment

### 4.2.4.1 USEPA (1986b)

By using data from the 1986 NTP inhalation bioassay, USEPA (1986b) estimated inhalation unit risk ranging from  $2.9 \times 10^{-7}$  to  $9.5 \times 10^{-7} (\mu\text{g}/\text{m}^3)^{-1}$ , with a geometric mean equal to  $5.8 \times 10^{-7} (\mu\text{g}/\text{m}^3)^{-1}$ . The inhalation unit risk estimates were calculated on the basis of metabolized doses (based on total urinary excretion of metabolites) from pharmacokinetic studies in mice and humans. Refer to USEPA (1986b) for detailed information on their dosimetric adjustments and dose-response assessment.

### 4.2.4.2 Travis et al. (1989)

Travis et al. (1989) used a physiologically-based pharmacokinetic (PBPK) model for PCE to analyze the animal bioassay data from the 1986 NTP inhalation study. The GLOBAL83 version of the linearized, multistage model was applied to determine the dose-response relationship for PCE based on the incidence of hepatocellular carcinomas exhibited in female B6C3F1 mice resulting from the 1986 NTP inhalation bioassay. Female B6C3F1 mice were considered the most sensitive strain with the most statistically sensitive tumor site among the NTP bioassay data. The 95% upper bound cancer potency factors in humans were calculated based on the equivalent effective dose of PCE in female B6C3F1 mice. The equivalent effective dose (lifetime averaged metabolized dose in the liver) was measured by either mg metabolite/kg body weight (BW) per day or mg metabolite/m<sup>2</sup> body surface area (SA) per day. A 95% upper bound potency factor of  $1.0 \times 10^{-2} (\text{mg}/\text{kg}\text{-day})^{-1}$  was computed using BW interspecies dose extrapolation. A 95% upper bound potency factor of  $1.4 \times 10^{-1} (\text{mg}/\text{m}^2\text{-day})^{-1}$  was also computed using SA interspecies dose extrapolation. These potency values and the PBPK model estimation of metabolized dose to the liver were then used to calculate a pharmacokinetically derived estimate of human risk associated with  $1 \mu\text{g}/\text{m}^3$  PCE in air. The 95% upper bound cancer potency was calculated using BW interspecies dose extrapolation to yield a unit risk factor (URF) of  $3.1 \times 10^{-7} (\mu\text{g}/\text{m}^3)^{-1}$ . A URF of  $4.3 \times 10^{-6} (\mu\text{g}/\text{m}^3)^{-1}$  was calculated when body surface scaling to the 2/3 power ( $\text{BW}^{0.67}$ ) was used. While the use of a SA correction is considered to be better than BW as the basis for interspecies dose extrapolation, the recent USEPA cancer guidelines (USEPA 2005a) indicate that when pharmacokinetic tissue dosimetry is used in a risk assessment, no body SA scaling should be performed. Thus, the Travis et al. (1989) URF of  $3.1 \times 10^{-7} (\mu\text{g}/\text{m}^3)^{-1}$  calculated using BW interspecies dose extrapolation has higher confidence than that calculated using body surface scaling.

### 4.2.4.3 OEHHA (1997)

The California Environmental Protection Agency (CalEPA) Office of Environmental Health Hazard Assessment (OEHHA) has published an inhalation URF of  $5.9 \times 10^{-6} (\mu\text{g}/\text{m}^3)^{-1}$  (OEHHA 1997). The estimated inhalation URF conducted by the California Department of Health Services (CDHS, 1991) was also based on a cancer risk assessment of the NTP (1986) inhalation bioassay study in mice and rats. CDHS used a PBPK model to predict metabolized dose by assuming humans metabolize 25% of absorbed PCE for each data set from the NTP cancer bioassays. However, considering that only 1-3% of the absorbed PCE is metabolized by humans, and that the metabolism of PCE is saturable, the CalEPA value may be conservative (Clewell et al. 2005).

#### 4.2.4.4 Preferred Model

In a case study, Clewell et al. (2005) performed a comparison of the ability of six various published human PBPK models to predict the rate of metabolism of PCE using the results of a study by Volkel et al. (1998) (in Clewell et al. 2005). The Volkel et al. (1998) study provided data on the blood concentrations of PCE and its major metabolite, TCA, as well as on the urinary excretion of TCA, following exposure of 6 human subjects (3 males and 3 females) to lower exposure concentrations of 10, 20, or 40 ppm PCE for 6 h. The results showed that all of the human models overpredicted the urinary excretion of TCA in the Volkel et al. (1998) study, ranging from a factor of 2 for the model of Gearhart et al. (1993) (in Clewell et al. 2005) to a factor of 10 for the model of Reitz et al. (1996) (in Clewell et al. 2005). The authors concluded that metabolism estimates obtained with the model of Gearhart et al (1993). would provide the most reliable dose metrics for a PCE risk assessment.

Gearhart et al. (1993) developed a human PBPK model of PCE that includes two fat compartments in the parent chemical description, and also describes the kinetics of the principal metabolite, TCA. The parameters for the metabolism of PCE in the human were estimated by fitting the model to data on the time course of urinary excretion of TCA following inhalation to PCE, assuming that TCA represents 60% of the total PCE metabolism in the human. The model is the only human PBPK model of PCE to include a description of TCA kinetics. The kinetics information allows data on the time course of metabolite kinetics and excretion to be more readily used for metabolism parameter estimation or validation and reduces the uncertainty associated with the tendency in human studies to collect urine for too short a time to ensure that all of the metabolite has been excreted (Clewell et al. 2005).

The Gearhart et al. model provided the closest predictions of the urinary excretion observed in low-concentration exposures. Other models overestimated metabolite excretion by 5- to 15-fold. Since the model of Gearhart et al. (1993) provides the most reliable dose metrics for a PCE risk assessment, it was preferred as the model of choice for the PCE risk assessment. Based on liver tumors in mice in the NTP inhalation bioassay, Clewell et al. (2005) used the Gearhart et al. (1993) model, lifetime average amount metabolized in the liver per unit liver weight as the dose metric, and the conservative linear low-dose extrapolation default approach (USEPA 2005a) to estimate the inhalation risk for PCE.

#### 4.2.5 Calculation of Air Concentration at $1 \times 10^{-5}$ Excess Cancer Risk

The resulting inhalation URF estimate for lifetime exposure based on the Gearhart et al. (1993) model is  $3.8 \times 10^{-7}(\mu\text{g}/\text{m}^3)^{-1}$ , which is very similar to the URF of  $3.1 \times 10^{-7}(\mu\text{g}/\text{m}^3)^{-1}$  calculated by Travis et al. (1989) and the URF of  $5.8 \times 10^{-7}(\mu\text{g}/\text{m}^3)^{-1}$  estimated by EPA (USEPA 1986). By using the Clewell et al. (2005) inhalation URF of  $3.8 \times 10^{-7}(\mu\text{g}/\text{m}^3)^{-1}$ , PCE's  $\text{chronicESL}_{\text{linear(c)}}$  at TCEQ's no significant risk level of  $1 \times 10^{-5}$  is calculated below:

$$\text{chronicESL}_{\text{linear(c)}} = [1 \times 10^{-5}] / [3.8 \times 10^{-7}(\mu\text{g}/\text{m}^3)^{-1}] = 26 \mu\text{g}/\text{m}^3 \text{ or } 3.8 \text{ ppb}$$

#### 4.2.6 Comparison of Various Cancer Potency Values

Table 5 is a comparison of the inhalation URF and  $\text{chronicESL}_{\text{linear(c)}}$  to URFs and toxicity values derived by other federal and state agencies.

<b>Table 5. Comparison of PCE Inhalation URFs and Chronic Toxicity Benchmarks</b>		
	Inhalation URF <sup>a</sup>	Chronic Toxicity Benchmark <sup>b</sup>
chronic <sub>ESL</sub> linear(c)	$3.8 \times 10^{-7} (\mu\text{g}/\text{m}^3)^{-1}$	26 $\mu\text{g}/\text{m}^3$ (3.8 ppb)
Clewell et al. (2005)	$3.8 \times 10^{-7} (\mu\text{g}/\text{m}^3)^{-1}$	26 $\mu\text{g}/\text{m}^3$ (3.8 ppb)
USEPA (1986b)	$5.8 \times 10^{-7} (\mu\text{g}/\text{m}^3)^{-1}$	34 $\mu\text{g}/\text{m}^3$ (5 ppb)
OEHHA (1997)	$5.9 \times 10^{-6} (\mu\text{g}/\text{m}^3)^{-1}$	1.7 $\mu\text{g}/\text{m}^3$ (0.25 ppb)
Travis et al. (1989)	$3.1 \times 10^{-7} (\mu\text{g}/\text{m}^3)^{-1}$ <sup>c</sup>	32 $\mu\text{g}/\text{m}^3$ (4.8 ppb)
Travis et al. (1989)	$4.3 \times 10^{-6} (\mu\text{g}/\text{m}^3)^{-1}$ <sup>d</sup>	2.3 $\mu\text{g}/\text{m}^3$ (0.34 ppb)
<sup>a</sup> All URFs were estimated based on a cancer risk assessment on the NTP (1986) inhalation bioassay study <sup>b</sup> Air concentration corresponding to cancer risk level of $1 \times 10^{-5}$ <sup>c</sup> URF calculated using body weight interspecies dose extrapolation <sup>d</sup> URF calculated using body surface scaling		

## 4.2.7 Evaluating Susceptibility from Early-Life Exposures

USEPA (2005b) provides default age-dependent adjustment factors (ADAFs) to account for potential increased susceptibility in children due to early-life exposure when a chemical has been identified as acting through a mutagenic MOA for carcinogenesis. However, PCE is not a chemical which is currently identified by USEPA as having a mutagenic MOA as discussed in Section 4.2.1. In addition, genotoxicity tests of PCE by the NTP found that it was not mutagenic in *Salmonella typhimurium* or in L5178Y/TK+/- mouse lymphoma cells tested with and without metabolic activation.

## 4.3 Welfare-Based Chronic ESL

### 4.3.1 Vegetation Effects

Possible effects of PCE on plants, especially for conifers, have been investigated by Frank and Frank (1985, 1986) and the Bavarian State Ministry (in European Union 2005). Bleaching of chlorophyll and phytolysis were observed in these studies. However, there were several drawbacks in these studies such as the uses of direct UV radiation, uncontrolled exposures, and possible presence of other pollutants (sulfur dioxide and nitrogen dioxide); the authors concluded that it was not possible to derive statistical values from the aforementioned studies.

#### 4.3.1.1 Plant Research International (2000)

In another study, the direct effects of PCE on plants was conducted by Plant Research International (2000) (in European Union 2005) using open-top chambers. Twelve plant species, representing a range of European flora, were chosen for this study. The overall range of seasonal average exposure levels was 7 – 2,140  $\mu\text{g}/\text{m}^3$ . The exposures were terminated for each species when the plants had flowered and developed seed. The overall range of exposure durations was 6 weeks – 6 months. The measured response

parameters, including numbers of flowers, pods, ears and berries, and the weight of biomass, were made at the end of exposures for the different species. The concentrations used in the derivation of effects concentrations are those over the exposure duration up to the point at which the relevant observations was made. The no observed effects concentration (NOEC) values were derived from the highest concentrations tested where the effects in the exposed group was not significantly different from that in controls. The results of the NOEC values for the most sensitive endpoint for each plant species are summarized in Table 6. The lowest NOEC of 46  $\mu\text{g}/\text{m}^3$  identified by exposure of PCE to bean and the endpoint was production of seed pod. The bean and effects of pod dry weight were considered most sensitive among tested plant species and endpoints. The lowest observed effects concentration for the pod dry weight for the bean was 82  $\mu\text{g}/\text{m}^3$  and was used to set the chronic vegetation-based ESL.

#### 4.3.1.2 Mode-of-Action Analysis

The chronic effects of PCE on plants has not been clearly established but may be related to the formation of TCA in the plant after uptake of PCE from the air. The results of the Plant Research International (2000) study (in European Union 2005) showed that TCA was found in significant amounts in all four species analyzed (pine, spruce, bean and kale). The highest concentrations were found in conifer needles, with levels up to 1,000 fold those reported for samples collected in the field.

Plant Species	Exposure Period	Endpoint	NOEC
Bean	6 weeks	Pod dry weight	46 $\mu\text{g}/\text{m}^3$
Wheat	11 weeks	Ear dry weight	747 $\mu\text{g}/\text{m}^3$
Kale	12 weeks	Stem dry weight	758 $\mu\text{g}/\text{m}^3$
Spruce	6 months	Foliar injury	109 $\mu\text{g}/\text{m}^3$
Pine	6 months	Foliar injury	109 $\mu\text{g}/\text{m}^3$
Beech	6 months	Foliar injury	750 $\mu\text{g}/\text{m}^3$
White Clover	6 weeks	Shoot dry weight	543 $\mu\text{g}/\text{m}^3$
Purple Moor Grass	6 months	Senescence	109 $\mu\text{g}/\text{m}^3$
Blue Berry	4 months	Senescence	109 $\mu\text{g}/\text{m}^3$
Haircap Moss	4 months	Post-exposure-growth	2,101 $\mu\text{g}/\text{m}^3$
Schreber's Moss	4 months	Post-exposure-growth	984 $\mu\text{g}/\text{m}^3$
Goose Neck Moss	4 months	Post-exposure-growth	2,101 $\mu\text{g}/\text{m}^3$

#### 4.3.1.3 Derivation of the Vegetation-Based Chronic ESL ( $^{\text{chronic}}\text{ESL}_{\text{veg}}$ )

Vegetation-based ESLs are set at the threshold concentration for adverse effects and are determined in accordance to ESL Guidelines (TCEQ 2006). The  $^{\text{chronic}}\text{ESL}_{\text{veg}}$  for PCE is therefore derived based on the

lowest observed effects concentration of  $82 \mu\text{g}/\text{m}^3$  identified by exposure of PCE to bean. Accordingly, the  $\text{chronic ESL}_{\text{veg}}$  of  $82 \mu\text{g}/\text{m}^3$  (12 ppb) for long-term exposures was therefore determined from the studies on bean (see Section 4.3.1.2).

#### ***4.4 Long-Term ESL and Values for Air Monitoring Evaluation***

This chronic evaluation resulted in the derivation of the following chronic values:

- chronic ReV =  $370 \mu\text{g}/\text{m}^3$  (54 ppb)
- $\text{chronic ESL}_{\text{nonlinear(nc)}} = 110 \mu\text{g}/\text{m}^3$  (16 ppb)
- $\text{chronic ESL}_{\text{veg}} = 82 \mu\text{g}/\text{m}^3$  (12 ppb)
- URF =  $3.8 \times 10^{-7} (\mu\text{g}/\text{m}^3)^{-1}$  ( $2.6 \times 10^{-6}$  per ppb)
- $\text{chronic ESL}_{\text{linear(c)}} = 26 \mu\text{g}/\text{m}^3$  (3.8 ppb)

The long-term ESL for air permit evaluations is the  $\text{chronic ESL}_{\text{linear(c)}}$  of  $26 \mu\text{g}/\text{m}^3$  (3.8 ppb) as it is lower than the  $\text{chronic ESL}_{\text{nonlinear(nc)}}$  or  $\text{chronic ESL}_{\text{veg}}$  (Table 1). For evaluation of air monitoring data, the  $\text{chronic ESL}_{\text{linear(c)}}$  of  $26 \mu\text{g}/\text{m}^3$  (3.8 ppb) is lower than the  $\text{chronic ESL}_{\text{veg}}$  of  $82 \mu\text{g}/\text{m}^3$  (12 ppb) and the chronic ReV of  $370 \mu\text{g}/\text{m}^3$  (54 ppb), although these three values may be used for the evaluation of air data (Table 1). The  $\text{chronic ESL}_{\text{nonlinear(nc)}}$  (HQ = 0.3) is not used to evaluate ambient air monitoring data.

## **Chapter 5 References**

### ***5.1. References Cited in DSD***

- Agency for Toxic Substances and Disease Registry (ATSDR 1997). Toxicological profile for Tetrachloroethylene (Update). U.S. Department of Health and Human Services Public Health Service. Atlanta, GA. Available from: [www.atsdr.cdc.gov/toxprofiles](http://www.atsdr.cdc.gov/toxprofiles).
- American Conference of Governmental Industrial Hygienists (ACGIH 2001). Documentation of the threshold limit value for tetrachloroethylene. ACGIH, Cincinnati, OH.
- Altmann, L, H Weigand, A Bottger, et al. 1992. Neurobehavioral and neurophysiological outcome of acute repeated tetrachloroethylene exposure. *Apply Psychol Int Rev* 41:269-279.
- Altmann, L, HF Neuhann, U Krame, et al. 1995. Neurobehavioral and neurophysiological outcome of chronic low-level tetrachloroethylene exposure measured in neighborhoods of dry cleaning shops. *Environmental Research* 69:83-89.
- California Department of Health Services (CDHS). 1991. Health effects of tetrachloroethylene (PCE). Technical support document: Proposed identification of perchloroethylene as a toxic contaminant. Part B. Berkeley, CA.
- ChemIDplus Advanced, Physical Properties for Tetrachloroethylene (RN: 127-18-4), <http://chem.sis.nlm.nih.gov/chemidplus/jsp/common/PhysicalProperties.jsp?calledFrom=lite>. U.S. National Library of Medicine.
- Clewell, HJ, PR Gentry, JE Kester, et al. 2005. Evaluation of physiologically based pharmacokinetic models in risk assessment: An example with perchloroethylene. *Critical Rev Toxicol* 35:413-433.
- European Union. 2005. Risk Assessment Report. Tetrachloroethylene. Part I - Environment. Institute for Health and Consumer Protection. European Chemicals Bureau. Vol.: 57. European Commission.
- Ferroni, C, L Selis, A Mutti, et al. 1992. Neurobehavioral and neuroendocrine effects of occupational

- exposure to perchloroethylene. *Neurotoxicology* 13:243-248.
- Leonardos, G, D Kendall, and N Barnard. 1969. Odor threshold determinations of 53 odorant chemicals. *J Air Pollution Control Assoc* 19(2):91-95.
- Lyngge, E., A Anderson, A Rylander, et al. 2006. Cancer in persons working in dry cleaning in the Nordic countries. *Environ Health Perspectives* 114: 213-219.
- May, J. 1966. An odor evaluation apparatus for field and laboratory use. *Am Ind Hyg Assoc J* 19:1-17.
- Mundt, KA, T Birk, and MT Burch. 2003. Critical review of the epidemiological literature on occupational exposure to perchloroethylene and cancer. *Int Arch Occup Environ Health* 76: 473-491.
- Nagata, Y. 2003. Measurement of odor threshold by triangle odor bag method. Odor Measurement Review, Japan Ministry of the Environment. pp. 118-127.
- National Toxicology Program (NTP 1986): Toxicology and carcinogenesis of tetrachloroethylene (perchloroethylene) in F344/N rats and B6C3F1 mice (Inhalation Studies). NTP TR 311. NTP, Research Triangle Park, NC.
- Office of Environmental Health Hazard Assessment (OEHHA 1997). Tetrachloroethylene. Toxic air contaminant identification list summary, pp. 889-893. California Environmental Protection Agency, Berkeley, CA.
- Rowe, VK, DD McCollister, HC Spencer , et al. 1952. Vapor toxicity of tetrachloroethylene for laboratory animals and human subjects. *AMA Arch Ind Hyg Occup Med* 5: 566-579.
- Stewart, RD, ED Baretta, and HC Dodd. 1970. Experimental human exposure to tetrachloroethylene. *Arch Environ Health* 20: 224-229.
- Travis, CC, RK White, and AD Arms. 1989. A physiologically based pharmacokinetic approach for assessing the cancer risk of tetrachloroethylene. In: Paustenbach, D.J. ed. *The Risk assessment of environmental and human health hazards: A Textbook of case Studies*. John Wiley & Sons, New York. pp. 769-796.
- United States Environmental Protection Agency. (USEPA 1986a). Guidelines for Carcinogen Risk Assessment. Federal Register 51(185): 33992-34003.
- United States Environmental Protection Agency (USEPA 1986b). Addendum to the health assessment document for tetrachloroethylene. Updated carcinogenicity assessment for tetrachloroethylene. EPA/600/8-82-005FA. Washington, D.C.
- United States Environmental Protection Agency (USEPA 2003). Neurotoxicity of Tetrachloroethylene (Perchloroethylene): Discussion Paper, EPA/600/P-03/005A. Washington, D.C. Available from: <http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=75193>
- United States Environmental Protection Agency. (USEPA 2005a). Guidelines for Carcinogen Risk Assessment. EPA/630/P-03/001B. Risk Assessment Forum. Washington, D.C.
- United States Environmental Protection Agency. (USEPA 2005b). Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens. EPA/630/R-03/003F. Risk Assessment Forum. Washington, D.C.
- Verschueren, K. 2001. Handbook of environmental data on organic chemicals, 4<sup>th</sup> ed., Van Nostrand Reinhold, New York.

## ***5.2. Other References Reviewed by TS***

- Covinton, TR, PR Gentry, CB Van Landingham, et al. 2007. The use of Markov chain Monte Carlo uncertainty analysis to support a public health Goal for perchloroethylene. *Reg Toxicol Pharmacol* 47: 1-18.

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Office of Environmental Health Hazard Assessment (OEHHA). March 1999. Acute toxicity summary for perchloroethylene in determination of acute reference exposure levels for airborne toxicants. California Environmental Protection Agency, Berkeley, CA. C267-C271.